Beat-to-beat variability of T-wave in multichannel magnetocardiogram and 12-lead electrocardiogram during physiological interventions

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1 Introduction

The autonomic nervous system regulates cardiac function by modulating heart rate and cardiac contractility. Changes in sympathetic and parasympathetic activity have effects on the amplitude and duration of the cardiac action potentials and conduction velocity. So far, no studies have been published on changes in MCG caused by rapid autonomic adaptation. For clinical applications of MCG it is important to clarify whether interventions involving changes in autonomic activity produce distinct changes in the MCG signal. Autonomic function tests cause fast adaptation in the cardiovascular system. Therefore, monitoring the change in the MCG signal beat by beat is essential in the analysis of the data recorded.

In this study we test the feasibility of MCG recordings during several simple, non-invasive physiological interventions affecting cardiovascular autonomic function and thoracic geometry in different manners. We also present an analysis method for extracting magnetic field maps from each cardiac cycle of the raw data and quantifying their change. We apply the method in the MCG data recorded, and examine the dynamic changes in magnetic field maps. In stress studies, the T-wave inversion in MCG of healthy subjects, not detected in ECG, has been of great interest. Therefore, the analysis is focused on the T-wave.

2 Methods

2.1 Measurements

The study population comprised of ten young male subjects (age 21 - 33 years) with no history of cardiovascular disease. The 67 channel cardiomagnetometer of the Biomag Laboratory in Helsinki University Central Hospital was used for the measurements, and simultaneous 12-lead electrocardiogram (ECG) was recorded. All subjects underwent six different recordings. 1) Normal breathing with controlled rate of 12 cycles/minute. 2) Mental stress by verbal arithmetic exercises: Subject subtracted 17 or 13 from a four digit number while loud beeps at 2 Hz frequency were given for distraction. The investigator urged the subject to faster performance and pointed out mistakes and too slow calculation. 3) Valsalva maneuver: The subject sustained an expiration pressure of 40 mmHg for 15 seconds in a tube, connected to a manometer outside the magnetically shielded room. 4) Sustained handgrip: The subject squeezed a non-magnetic dynamometer with 30 % of maximal strength for 5 minutes. Breathing frequency was 12 cycles/minute. 5) Deep breathing: The subject respired with maximal vital capacity at 6 cycles/minute for 5 minutes. 6) Cold pressure test: the subject immersed his hand up to the wrist in +4 °C water for two minutes, while the breathing was rate controlled at 12 cycles/minute.

2.2 Data extraction

QRS complex detection An ECG channel with high signal amplitude was selected for automatic detection of the QRS complexes. First, a time point of the steepest signal slope was found in one beat and it was used as the template. By calculation of the highest signal correlation with the template, time instants at the same location in signal morphology were then found in all QRS complexes. These instants (the trigger times) were used for defining other time points of each cardiac cycle.

Baseline estimation Time from a trigger point to the beginning of a 20 ms baseline interval, as well as to the QRS onset and offset was defined in one cardiac cycle and used for all beats. A non-linear baseline estimate through the baseline points at the PQ intervals was calculated for all channels, and subtracted from the signal [1].

Magnetic field map extraction To extract magnetic field map (MFM) and ECG data of the T-wave apex from one cardiac cycle, the ST-T interval was first defined. Here, a rough estimate for the T-wave offset was obtained as $QRS\ onset + 450ms \cdot (RR - time)^{1/3}$ [2]. The T-wave apex time for each channel was derived as the highest signal deviation from the baseline within the ST-T interval. The median T-wave apex time over all channels was calculated to obtain the T-wave apex time for the whole data set. T-wave apexes of all cardiac cycles were found, and integral data over 21 ms around T-wave apex were extracted for further analysis. To make all MCG channels comparable with each other, data of planar and axial gradiometer units were converted to 33-channel data of axial gradiometers only [3].

Magnetic field map parametrization To quantify MFM amplitude, the highest and lowest signal value over the mapped area were found. The MFM polarity was quantified by the number of channels with a positive T-wave. Surface gradient method, reported earlier [4], was used to determine the orientations of the MFMs. Briefly, the location of the largest spatial change in the field distribution was first found. The angle between the direction of the field change at that point, and the patient's right-left line was then defined as the MFM angle.

Parameter data presentation Amplitude, polarity, and orientation data of each subject in each measurement were plotted against time and against time between two consecutive R deflections (RR-interval). Changes in the parameters, induced by different interventions, were evaluated qualitatively and further analysis was focused on the interventions and parameters with the largest change.

Quantification of change in the data To quantify the amplitude variation on each MCG and ECG channel during quiet and deep breathing, mean deviation of signal amplitude (mean difference between average amplitude and each amplitude value) was calculated on all channels. Variation was defined as 2 · mean deviation, and the channels with the largest variation were identified. Beat-to-beat variation in the MFM parameters (amplitude, polarity, and orientation) was quantified by calculating the value 2 · mean deviation in each parameter during the recording.

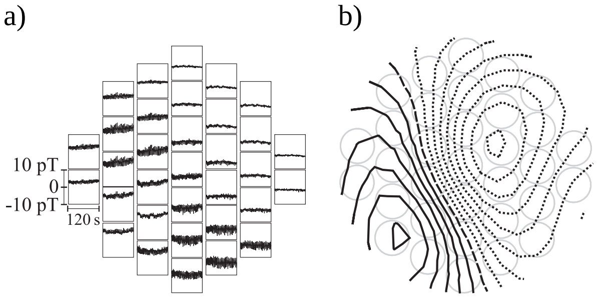

Figure 1: *a) T-wave apex amplitudes of all cardiac cycles in a 120 s recording during deep breathing. Data of the 33 channel setup are presented. b) Magnetic field map integrated over the T-wave apex of 25 cardiac cycles (2 breathing cycles). The most extensive beat-to-beat variation in a) takes place near the zero-field line denoted by a dashed line in b).*

Heart rate dependence of the MFM parameters during mental stress was evaluated by fitting a regression line in the parameter vs. RR-interval -data. Line slope quantified the change. In the other tests, changes in MFM parameters were evaluated only qualitatively.

3 Results

Table 1 shows the mean change in heart rate during different interventions. Valsalva maneuver and mental stress induced highest elevations in the heart rate. In the Valsalva test, after tachycardia during strain, the typical bradycardia followed with mean heart rate of 46±5 beats per minute (bpm).

3.1 Quiet and deep breathing

In the MCG, the highest T-wave amplitude variation both during quiet and deep breathing was found on channels close to the zero field line (see Fig. 1). During quiet breathing, the mean variation was 2.0±1.3 pT and during deep breathing it was

Table 1: *The heart rates (beats per minute) during autonomic function tests.*

Test	Baseline	Max HR
Mental stress	68±7	100±16
Valsalva	62±7	103±14
Handgrip	65±6	78±9
Deep breathing	58±8	75±8
Cold pressure	60±8	77±12

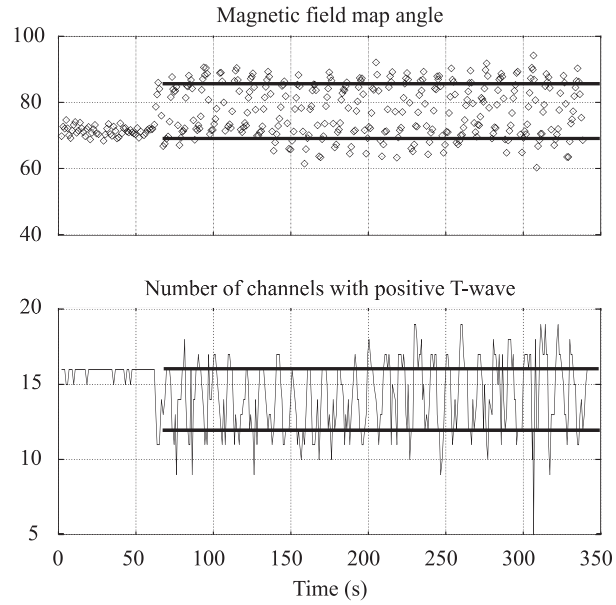

Figure 2: *The magnetic field map angle (above) and the number of channels with positive T-wave (below) of one subject during quiet (60 first seconds of data) and deep breathing. Thick horizontal lines indicate the interval quantifying the variation in the parameters due to deep breathing.*

4.0±2.6 pT. In the ECG, the highest variation was typically found on leads V1 and V2 with mean variation of 80±30 μV during quiet, and 240±130 μV during deep breathing. The variation in the MFM angle due to quiet and deep breathing was 6.4±6.3° and 13.7±6.9°, respectively (see Fig. 2). During quiet breathing on average, 16±3 of the 33 channels had a positive T-wave and variation in their number was 1.8±0.5 channels. During deep breathing the values were 15±2.3 and 3.5±1.3 channels, respectively (Fig. 2).

3.2 Mental stress

Decrease in the RR-interval due to mental stress resulted in a counter-clockwise MFM rotation in eight of the ten volunteers studied, and in two subjects the maps rotated clockwise. Two subjects had MFM angle / RR-interval slope steeper than -0.05°/ms but in other eight subjects it was milder, on average $-0.013 \pm 0.014^\circ$/ms. In qualitative observation, mental stress had only small effect on the amplitude of the field extrema in most subjects, and the number of channels with positive T-waves was the same or only little smaller than at rest.

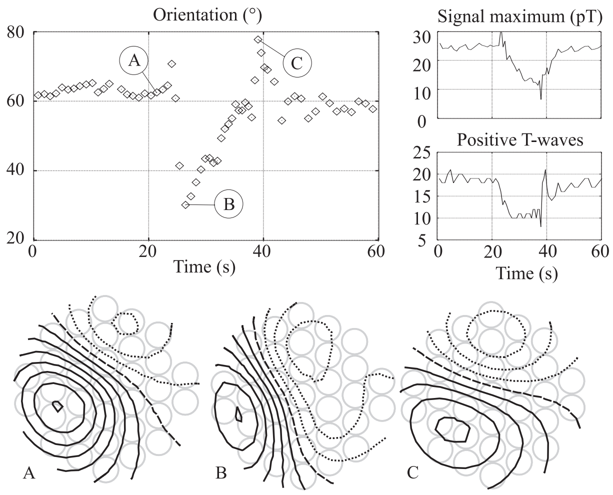

Figure 3: *MCG parameters and examples of magnetic field maps of the T-wave during the Valsalva maneuver. Above, the large panel shows the MFM orientation, and in the small figures maximum value of the MCG signal over the mapped area, as well as the number of channels with a positive T-wave are plotted against time. The time instants and orientation values of the maps presented are indicated in the orientation data.*

3.3 Valsalva maneuver

During the Valsalva maneuver the orientation, amplitude, and polarity parameters showed a consistent development in all subjects. At the beginning of the strain, the MFM rotated clockwise, the field extrema damped, and the number of channels with a negative T-wave increased (see Fig. 3). At cessation of blowing, parameters recovered to the value at rest. In the MFM orientation, a counter-clockwise overshoot took place before recovery (Fig. 3).

3.4 Handgrip and cold pressure test

In qualitative observation, the changes induced by sustained handgrip and the cold pressure test in the MCG were smaller than those due to Valsalva maneuver and deep breathing.

4 Discussion

The heart rate responses to the autonomic function tests performed in this study agreed with those reported in the literature, indicating that the interventions used were adequate.

The most striking alterations in the T-wave amplitude due to deep breathing, including polarity changes, were found on channels close to the spatial zero-field line. As expected, T-wave inversions were not found in the ECG. The spatial gradient of the MCG signal during the T-wave was highest near the zero-field line, and movement of the heart along the gradient would induce the largest change in the signal on these locations. In body surface potential mapping, the largest spatial potential gradient during the T-wave is typically located close to leads V1 and V2, where the largest T-wave amplitude variation was found also in this work. These findings support the hypothesis that change in the location of the heart is one element underlying the change in T-wave polarity on the central MCG channels during heavy breathing. However, contribution of other factors, e.g. changes in cardiac volume, can not be excluded.

Of all tests performed, the Valsalva maneuver induced the most consistent and extensive changes in the MFMs at the T-wave. In addition to inversion of T-waves from positive to negative on some channels, the MFMs rotated during the test. The Valsalva strain consists of forced expiration against resistance, causing a significant increase in intrathoracic pressure. This reduces venous return from outside the thorax, causing depressed cardiac output and diminished blood pressure, eliciting a reflex increase in heart rate. After the release of the strain, the increased heart rate and restored venous return cause a rebound hypertension and reflex bradycardia. In qualitative evaluation, the development in the MFM angle was found to correlate with the strain phase; the initiation of the strain was associated with a rapid and marked clockwise MFM rotation. As the forced expiration continued the MFM angle gradually recovered to baseline value, after a small overshoot (Fig. 3). It is unlikely that the changes in heart rate and autonomic activity are solely responsible for the MFM rotation. Movement of the heart with respect to chest wall and the respiration pattern during the maneuver probably contribute to the observed changes. Actual repolarization changes may also be brought about by changes in cardiac volume and myocardial tension.

5 Conclusion

In this paper we describe the magnetocardiographic response to several autonomic function tests in healthy young male subjects. Changes found during the handgrip test and cold pressure test were minor. The effect of mental stress was also small, but in two healthy subjects significant T-wave alterations were described. Thus, non-specific T-wave changes may occur in subjects without known heart disease during sympathetic stimulation induced in this manner.

In any MCG study involving interventions, attention should be paid to possible confounding effects of breathing and maneuvers causing changes in intrathoracic volume and pressure conditions. The beat-to-beat analysis method introduced, enables monitoring of magnetic field maps and quantification of change in the MCG during dynamic studies. The MCG measurements during the interventions studied, and their analysis were found to be feasible and the results encourage patient measurements during autonomic function tests.

References

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